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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,963	07/15/2003	Preben Lexow	Q76325	5915

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EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
09/02/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/618,963	LEXOW, PREBEN	
	Examiner	Art Unit	
	Ethan Whisenant	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,29-35 and 40- 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,29-35 and 40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/866,223.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL ACTION

1. **A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed on 22 AUG 07 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.** Claim(s) 26, 29-35 and 40-42 **is/are now pending. 35 USC § 112 - 1ST PARAGRAPH**

Deleted: ¶

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim REJECTIONS under 35 USC § 112- 1ST PARAGRAPH

3. Claims 26, 29-35 and 40-42 is/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the Claimed invention. This is a new matter rejection. The new matter added is the negative limitation in Claims 26 and 42 which reads "wherein the label which indicates the position of said portion of the nucleic acid molecule is not used to determine the sequence of said portion". It is well established that there is nothing inherently ambiguous or uncertain about a negative limitation. However, it is also well established [see *Ex parte Graciously* 231 USPO 393 (Bd App. 1983)] that any negative limitations or exclusionary proviso must have basis in the original disclosure. The mere absence of a positive recitation is not basis for exclusion. The MPEP at 2163.06 teaches : "If new matter is added to the Claims, the examiner should reject the Claims under 35 U.S.C. 112, 1st paragraph – written description requirement. In re Rassmussen, 650 F.2D 1212, 211 USPQ 323 (CCPA

1981)." The MPEP at 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a Claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. If a Claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the Claimed subject matter is not described in that application." It is noted that the applicant has pointed to Example 21 which begins on p.95 of specification, for support for the negative limitation, however, the examiner fails to see where in Example 21 where there is explicit support for the negative limitation.

35 USC § 112- 2ND PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

5. **Claim(s) 31 and 40** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is indefinite because the phrase “assessing said complementary ” is non-sequitur. Perhaps the word complementarity would be more appropriate.

Claim 40 is indefinite because the phrase “said magnifying” at least one gene” lacks proper antecedent basis in Claim 26..

35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

CLAIM REJECTIONS UNDER 35 USC § 102/103

8. Claim(s) 26, 29 and 41-42 is/are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Reeders et al. [US 6,007,980(1997)].

Claim 26 is drawn to a method of sequencing all or part of a target nucleic acid molecule, said method comprising determining the sequence of a portion of said target nucleic acid molecule wherein the position of said portion within said target nucleic acid molecule is determined by identifying a label which is associated with said portion of the target nucleic acid molecule and which indicates the position of said portion within the target nucleic acid molecule, wherein the sequence and position information obtained is combined in order to obtain the sequence of said target nucleic acid molecule, wherein the label which indicates the position of said portion within the target nucleic acid molecule is not used to determine the sequence of said portion, and wherein the portion which is sequenced has 2 or more bases.

Reeders et al. teach a restriction enzyme map and a method of sequencing all or part of a target nucleic acid molecule, said method comprises determining the sequence of a portion of said target nucleic acid molecule using the Sequenase method (i.e. the Sanger/dideoxy method). See for example Figure 9. Reeders et al. do not explicitly teach determining the position of said portion within the target nucleic acid molecule by identifying a label which is associated with said portion and which identifies the position of said portion within the target nucleic acid molecule. However, it was well known (Official Notice) to use restriction enzyme sites as alignment landmarks (i.e. as labels) in sequencing methods. For example, consider lines 3-12 of Column 2 on p. 3390 of Cai et al. [PNAS 95 : 3390-3395 (MAR 1998)]. There, Cai et al. teach the utility of restriction enzyme sites/maps to serve as markers (I.e. as labels) in facilitating sequence read alignments in sequencing projects. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the

art at the time of the invention to utilize the positional information generated by the restriction map of Reeders et al. in combination with the primary nucleotide sequence information generated by the method Reeders et al. to determine the position of a given portion (i.e. a given subclone's sequence) within the larger target nucleic acid molecule. Note that in Reeders et al. the label which indicates the position of portion [i.e. the restriction enzyme site(s)] within the target is not the label used to determine the sequence of said portion(i.e. ^{32}P label taught by Sanger et al., [PNAS 74(12) : 5463-5467 (1977)]. Finally note that the portion sequenced has 2 or more bases, see Figure 9.

Claim 29 is drawn to an embodiment of the method of Claim 26 wherein the portion which is sequenced has four or more bases and/or the position of said portion within said target nucleic acid molecule is determined to be with an accuracy of less than 1 kb.

Reeders et al. teach both of these limitations, see at least for example Figure 9.

Claim 41 is drawn to an embodiment of the method of Claim 26 wherein said label is or comprises a polynucleotide.

Reeders et al. teach both of these limitations. Note that each restriction enzyme site (i.e. a label of Reeders) are composed of a polynucleotide sequence, see at least, for example Figure 9.

Claim 42 is drawn to a method of sequencing all or part of a target nucleic acid molecule, said method comprising determining the sequence of a portion of said target nucleic acid molecule wherein the position of said portion within said target nucleic acid molecule is determined by identifying a label which is associated with said portion of the target nucleic acid molecule and which indicates the position of said portion within the target nucleic acid molecule, wherein the sequence and position information obtained is combined in order to obtain the sequence of said target nucleic acid molecule, wherein the label which indicates the position of said portion within the target nucleic acid molecule is not used to determine the sequence of said portion, and wherein the portion which is sequenced has 2 or more bases.

Reeders et al. teach a restriction enzyme map and a method of sequencing all or part of a target nucleic acid molecule, said method comprises determining the sequence of a portion of said target nucleic acid molecule using the Sequenase method (i.e. the Sanger/dideoxy method). See for example Figure 9. Reeders et al. do not explicitly teach determining the position of said portion within the target nucleic acid molecule by identifying a label which is associated with said portion and which identifies the position of said portion within the target nucleic acid molecule. However, it was well known (Official Notice) to use restriction enzyme sites as alignment landmarks (i.e. as labels) in sequencing methods. For example, consider lines 3-12 of Column 2 on p. 3390 of Cai et al. [PNAS 95 : 3390-3395 (MAR 1998)]. There, Cai et al. teach the utility of restriction enzyme sites/maps to serve as markers (I.e. as labels) in facilitating sequence read alignments in sequencing projects. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize the positional information generated by the restriction map of Reeders et al. in combination with the primary nucleotide sequence information generated by the method Reeders et al. to determine the position of a given portion (i.e. a given subclone's sequence) within the larger target nucleic acid molecule. Note that in Reeders et al. the label which indicates the position of portion [i.e. the restriction enzyme site(s)] within the target is not the label used to determine the sequence of said portion (i.e. ^{32}P label taught by Sanger et al., [PNAS 74(12) : 5463-5467 (1977)]. Finally note that the portion sequenced has 2 or more bases, see Figure 9.

CLAIM REJECTIONS UNDER 35 USC § 103

9. Claim(s) 30-33, 35 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Reeders et al. [US 6,007,980(1997)] as applied against Claim 26 above and further in view of Broude et al. [PNAS 91 : 3072-3076 (1994)].

Claim 30 is drawn to an embodiment of the method of Claim 26 wherein said portion is sequenced by identifying magnifying tags associated with the target nucleic acid molecule wherein said magnifying tags correspond to one or more bases of an adapter binding region or to one or more bases in proximity to an adapter binding region, wherein said adapter binding region binds an adapter molecule which comprises one or more magnifying tags or a means for attaching one or more magnifying tags. Reeders et al. teach a method of sequencing all or a portion target nucleic acid molecule which comprises all of the limitations set forth in Claim 30 except these authors do not teach identifying magnifying tags associated with the target nucleic acid molecule as is required by Claim 30. However, as evidenced by at least Broude et al. a method of sequencing a target nucleic acid molecule which comprises identifying magnifying tags as defined by Claim 30 was known. See especially Figure 1 and Table 5. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to substitute the method of sequencing disclosed by Broude et al. for the method of sequencing disclosed by Reeders et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09. In Broude et al. the magnifying tags are the nucleotide sequences detected as shown in Table 5 and note that the magnifying tags correspond to one or more bases of an adapter binding region. The adapter is the double stranded probe immobilized on the solid support as shown in Figure 1. This adapter of Broude et al. comprises a means (i.e. the 3' overhang sequence) for attaching one or more magnifying tags.

Claim 31 is drawn to an embodiment of the method of Claim 26 wherein the sequence of the target nucleic acid molecule is determined by assessing the complementary of a portion of said target nucleic acid molecule has four or more bases and/or the position of said portion within said target nucleic acid molecule by a process comprising three required steps. First the target nucleic acid molecule is treated such that at least a region of said target nucleic acid molecule is converted to a form suitable for binding a complementary probe wherein said complementary probe is bound to a solid support or carries a means for attaching to a solid support. Next said complementary probe is bound to at least a portion of said region suitable for binding a complementary probe. Finally, the sequence of said target nucleic acid molecule is determined by identifying the complementary probe(s) which bound to said target nucleic acid molecule.

Reeders et al. teach a method of sequencing all or a portion target nucleic acid molecule which comprises all of the limitations set forth in Claim 31 except these authors do not teach binding/detecting complementary probes to the target nucleic acid molecule as is required by Claim 31. However, as evidenced by at least Broude et al. a method of sequencing a target nucleic acid molecule comprising the steps recited in parts (i), (ii) and (iv) was known , see especially Figure 1 and Table 5. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to substitute the method of sequencing disclosed by Broude et al. for the method of sequencing disclosed by Reeders et al.

Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 32 is drawn to an embodiment of the method of Claim 31 wherein in step (i) said form is a single stranded nucleic acid molecule.

Broude et al. teach this limitation, see especially Figure 1.

Claim 33 is drawn to an embodiment of the method of Claim 31 wherein in step (ii) said is 4 to 12 bases in length.

Broude et al. teach this limitation, see especially Table 5. and note for each probe detected a sequence of 5 bases was determined.

Claim 35 is drawn to an embodiment of the method of Claim 26 wherein said method is performed on a sample comprising a heterogeneous mixture of target nucleic acid molecules.

Broude et al. teach this limitation, see especially the section on p. 3073 entitled "Preparation of Nested Target ".

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

10. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

11. **Claims 1, 3-5, 7, 10-18 and 20-30** is/are rejected and/or objected for the reason(s) set forth above.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30 am -5:30

pm EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

/Ethan Whisenant/
Primary Examiner
Art Unit 1634

EXAMINER SEARCH NOTES

27 AUG 10 09 - ECW

Databases searched: USPATFULL, USPG-PUBS, JAPIO and EUROPATFULL via EAST &

CAplus, Medline and BIOSIS via STN

Reviewed the parent(s), if any, and any search(es) performed therein : see the BIB data sheet

Reviewed, the search(es), if any, performed by prior examiners

Search terms:

Inventor(s) : e.g. Lexow P?/au

Sequence or Sequencing
DNA or Nucleic
Magnifying tag$
Label or labeled
Cycle or cycles

Adapter$

SBH or sequencing by hybridization